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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,121	05/16/2003	Karin Klokkers	4271-34PUS	8059

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EXAMINER	
GHALI, ISIS A D	
ART UNIT	PAPER NUMBER
1611	

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12/29/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/019,121	KLOKKERS ET AL.	
	Examiner	Art Unit	
	Isis A. Ghali	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-7 and 10-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-7 and 10-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The receipt is acknowledged of applicants' amendment and declaration, both filed 09/04/2008.

Claims 2, 8 and 9 have been canceled. Claims 20 and 21 have been added.

Claims 1, 3-7 and 10-21 are pending and are included in the prosecution.

The following rejection has been overcome by virtue of applicants' amendment and remarks:

Claims 1, 3-7, 10-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

The following rejection has been discussed in the previous office action, and maintained for reasons of record:

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1, 3-7 and 10-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of US 6,303,141 ('141) and EP 349 430 ('430).

US '141 teaches transdermal drug delivery device comprising backing layer, matrix containing 10% ACE inhibitor and Eutanol G as permeation enhancer, and protective release liner. The ACE inhibitor is at least one of ramipril or trandolapril in the acid form or active salts which encompass monosalts. The ACE inhibitor is present in the form of prodrug or active form, i.e. dicarboxylic acid, salts and esters (abstract; col.2, lines 25-30, 37-43; the claims).

Although US '141 teaches active salts and acid of ACE inhibitors, it does not specifically teach monosalts as claimed by claim 1. US '141 does not teach the cover over the backing layer that is larger than the backing as claimed by claims 14-17.

The cover sheet and its size do not impart patentability to the claims, absent evidence to the contrary.

EP '430 teaches a transdermal system that has improved flux through the skin achieved by using specific salt forms of the drug (page 2, lines 45-50). The transdermal system has a top layer, a layer containing ACE inhibitor, an adhesive layer and protective layer (page 3, lines 40-50). The reference also disclosed on page 3 lines 4-10 the salt forms of the drugs including methane sulphonate and dicarboxylate such as maleate. Example 1 shows that ACE inhibitors are present as monosalts such as libenzapril monomaleate.

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide transdermal system for delivery of salts of ACE inhibitors as disclosed by US '141, and replace the salt of ACE inhibitor by monosalts as disclosed by EP '430, motivated by the teaching of EP '430 that transdermal system that having monosalts ACE inhibitors showed improved flux through the skin, with reasonable expectation of having transdermal system for delivery of monosalts of ACE inhibitors at improved flux rates.

Response to Arguments

4. Applicant's arguments filed 12/27/2007 have been fully considered but they are not persuasive. Applicants' argue that US '141 does not teach monosalts. The term "therapeutically active salts" must be interpreted in view of EP '430. Applicants admit that EP '430 teaches dicarboxylic acid salts of ACE inhibitors, but still argue that EP

'430 teaches stoichiometric salts of ACE inhibitors and does not teach monosalts. The references do not teach that ACE inhibitors remain stable and exhibits outstanding skin permeation.

In response to above argument, applicants' attention is directed to the scope of the present claims that recites either monosalts or dicarboxylic acid diester. EP '430 teaches monosalts with acids. It is further argued the present claims are directed to product, and all the elements of the product are disclosed by the combined teaching of the prior art. On col.2, lines 26-28, US '141 teaches the use of ramipril or trandolapril in their active acid form or therapeutically active salt forms. Instant claim 20 encompasses wide range of salts including maleate and methane sulphonate. EP '430, in page 3 lines 4-10 of EP '430, teaches that the salt forms of the drugs include methane sulphonate and maleate, which claimed by claim 20. EP '430 teaches maleate and methane sulphonate of ACE inhibitors, and such salts re expected to have the same stability and skin permeability as the claimed salts since compounds and their properties are inseparable, specially in view of the disclosure of the references of the same transdermal device as claimed having same structure. In considering the disclosure of the reference, it is proper to take into account not only the specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of

ordinary skill in the art. The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve different problem. It is not necessary that the prior art suggest the combination or modification to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972).

It has been held that "When a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious." *KSR Int 'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740 (2007) (quoting *Sakraida v. AG Pro, Inc.,* 425 U.S. 273,282 (1976)). "When the question is whether a patent claiming the combination of elements of prior art is obvious," the relevant question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." In addition, "To determine whether there was an apparent reason to combine the known elements in the way a patent claims, it will often be necessary to look to interrelated teachings of multiple patents; to the effects of demands known to the design community or present in the marketplace; and to the background knowledge possessed by a person having ordinary skill in the art. To facilitate review, this analysis should be made explicit. But it need not seek out precise teachings directed to the challenged claim's specific subject matter, for a court can consider the inferences and creative steps a person of ordinary skill in the art would employ". Pp. 11-14. KSR INTERNATIONAL CO. v. TELEFLEXINC. ET AL. (2007). A conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable

expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969).

In the light of the foregoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the claims would have been *prima facie* obvious within the meaning of 35 U.S.C. 103 (a).

Response to Amendment

5. The declaration under 37 CFR 1.132 filed 09/04/2008 is insufficient to overcome the rejection of claims 1, 3-7, 10-21 based upon combination of US '141 and EP '430 as set forth in the last Office action because: the combination of the references would teach maleate salt and methane sulphonate of ACE inhibitors, which is the monosalts of ACE inhibitor with acid which are claimed by claim 20. The present claims requires (a) a dicarboxylic acid which is derivatised to form a diester, **OR** (b) a mono salt formed with acid(s). Claim 20 recites monosalts of organic or inorganic acids, fatty acids, aliphatic sulphonic acid and aromatic sulphonic acid and recites maleate and methane sulphonate that are described by EP '430. Applicants compared dicarboxylic diester with the monoester, while the scope of the claims further encompass monosalts with acids. Thus, there is no showing that the objective evidence of nonobviousness is commensurate in scope with the claims. See MPEP § 716. The scope of the claims is broad covering dicarboxylic diester and monosalts with acids while the declaration is limited to dicarboxylic diester. The single and specific species in the composition of the

declaration does not support the generic concept of the claims, especially in view of the teaching of EP '430 that encompasses some of the claimed species.

In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 6:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571) 272-0614. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

IG

/Isis A Ghali/
Primary Examiner, Art Unit 1611